

REMARKS

Applicants respectfully requests entry of the remarks submitted herein. No claims have been amended. Reconsideration of the pending application is respectfully requested.

The Specification

The disclosure was objected to because page 2 of the specification makes reference to claim numbers. The Examiner urged Applicants to delete the reference to claim numbers given that claim numbers are subject to change.

Applicants deleted this paragraph in the February 26, 2002 Preliminary Amendment filed with the application. Therefore, the Examiner's objection to the specification is moot.

The 35 U.S.C. §112 Rejection

Claims 1-13 stand rejected under 35 U.S.C. §112, first paragraph, as the Examiner asserted that those claims contain subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection is respectfully traversed.

The Examiner asserted that there were only two examples in the specification, and that neither example detected and quantified a biopolymer. The Examiner further asserted that the specification is silent as to how one would detect and quantify biopolymers that vary in base composition or where a highly heterogeneous mixture of biopolymers is present in the sample. According to the Examiner, given that biopolymers such as proteins and nucleic acids can undergo denaturation and degradation when subjected to electric fields, it is critical that the skilled artisan be provided with guidance as to what field strengths should be applied for different biopolymers, be they nucleic acids, proteins, lipids, or polysaccharides. The Examiner stated that the extent and specificity of hybridization is affected by numerous principal conditions and asserted that the specification is silent as to how art-recognized difficulties are to be overcome.

The test for enablement is whether one skilled in the art at the time Applicants filed the present application could make or use the claimed invention from the disclosures in the specification coupled with the information known in the art without “undue” experimentation. See, for example, MPEP.2164.01. According to *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)), many factual considerations must be weighed when determining whether “undue” experimentation would be required, including: (1) the breadth of the claims, (2) the nature of the invention, (3) the state of the prior art, (4) the relative skill of those in the art, (5) the predictability or unpredictability of the art, (6) the amount of direction or guidance provided, (7) the presence or absence of working examples, and (8) the quantity of experimentation necessary. It is improper to conclude that a disclosure is not enabling based on an analysis of only one of the above factors while ignoring one or more of the others. In other words, all the evidence related to each of these factors must be considered, and any conclusion of lack of enablement must be based on the evidence as a whole. MPEP.2164.01(a).

With respect to the breadth of the claims, the claims recite a method for detecting and quantifying biopolymers in a liquid. The specification discloses that the method “can be carried out simply and quickly” (page 2 lines 34-35). Applicants detected a DNA sequence encoding human growth hormone (HGH1) in a liquid solution using the methods of the invention with either direct voltage or alternating-current voltage. Figure 1 shows the results when direct voltage was used, and Figure 2 shows the results when alternating-current voltage was used. In addition, Figure 3 shows a diagrammatic representation of the methods of the invention. Applicants submit that the specification as written enables the breadth of the claims.

With respect to the nature of the invention, the invention relates to molecular biology.

With respect to the relative skill of those in the art, Applicants submit that the level of skill in the art is high. The specification discloses and exemplifies detecting and quantifying a biopolymer in a liquid solution. See, for example, Examples 1 and 2 and Figures 1 and 2. In addition, those of skill in the art know what field strengths to use in the methods of the invention with different biopolymers. See, for example, page 5, lines 14-21.

With respect to the state of the prior art, the prior art methods for detecting a biopolymer require the addition of particular redox-active molecules or chips. See, for example, page 1, lines 36-38. Quantification of a biopolymer in the prior art also requires optics, and cannot be

done in the manner in which quantification is described in the instant specification. See, for example, page 2, lines 1-3.

With respect to the predictability or unpredictability of the art, Applicants submit that the art applicable to the instant invention is not unpredicable. In addition, the predictability of being able to practice Applicants' invention is high. The specification discloses methods and various embodiments for detecting and quantifying a biopolymer in a liquid. See, for example, page 3, line 4 through page 5, line 21. The specification exemplifies methods that can be used to detect a biopolymer (e.g., DNA) in a liquid (see, for example, Examples 1 and 2). In addition, the specification includes Figure 3, which shows a diagrammatic view of the methods of the invention.

With respect to the amount of direction provided and the presence of working examples, Applicants provide a sufficient amount of direction in the specification for practicing the claimed methods. See, for example, page 3, line 4 through page 5, line 21. Examples 1 and 2 in the specification disclose using either direct voltage or alternating-current voltage to detect a nucleic acid encoding HGH1. In addition, Figure 3 shows a diagrammatic representation of the methods of the invention. The specification also discloses numerous embodiments of the invention. See, for example, page 3, line 4 through page 5, line 21.

With respect to the quantity of experimentation needed, Applicants submit that although there may be many biopolymers potentially detectable, the methods are routinely practiced by those in the art, are straightforward, and are described in the specification (see, for example, page 3, line 4 through page 5, line 21, Examples 1 and 2, and Figure 3). Enablement "is not precluded even if some experimentation is necessary, although the amount of experimentation needed must not be unduly extensive." *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 231 USPQ 81 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987).

Applicants' specification enables the full scope of the pending claims. In view of the amendments and remarks herein, Applicants respectfully request that the rejection of claims 1-13 under 35 U.S.C. §112, first paragraph, be withdrawn.

Claims 1-13 are rejected under 35 U.S.C. 112, first paragraph, as the Examiner asserted that those claims contain subject matter that was not described in the specification in such a way

as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse this rejection.

The Examiner asserted that the disclosure does not disclose any method whereby any biopolymer of any type was detected and quantified nor does the disclosure teach in sufficient detail how to make the genus of devices encompasses by the claims such that any biopolymer, regardless of composition, size, concentration and charge, would be detected and quantified by the disclosed method. The Examiner further stated that also missing is disclosure as to how the claimed method is to be practiced.

The Examples in the specification make it clear to a person skilled in this art the voltage or electromotive force that needs to be applied to detect and quantify the biopolymers. Further, Examples 1 and 2 clearly show that a DNA sequence, namely HGH1, can be detected by the claimed method. See Figures 1 and 2. The claimed method is based on the principal that upon hybridization of two complementary biopolymers, a capacitance is formed at the surface of an electrode. Due to such a capacitance being formed, the behavior of the electrode is changed. This change can be used to detect and quantify (first) biopolymers that are complementary to (second) biopolymers bound to the surface of the electrode. The Examples provided in the specification clearly demonstrate that Applicants had possession of the claimed invention at the time of filing.

In addition, the parameters for carrying out the invention are given in the Examples. The starting materials are identified. In particular, information about the applied voltage and the measurement methods used is disclosed. It is clear to a skilled person having knowledge about voltametric measurement methods that suitable standard field strengths are used to prevent a degradation of the biopolymers to be detected. Applicants note that the Examples were carried out as described and claimed (i.e., no additional steps are required).

The results shown in Figures 1 and 2 clearly demonstrate that Applicants possessed the claimed invention at the time of filing and, therefore, meet the written description requirement. Applicants respectfully request that the rejection of claims 1-13 under 35 U.S.C. §112, first paragraph, be withdrawn.

The 35 U.S.C. §102/103 Rejections

Claims 1-9 and 13 stand rejected under 35 U.S.C. §102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Thorp et al. (U.S. Patent 5,871,919). Applicants respectfully traverse this rejection.

According to the Examiner, Thorp et al., discloses detecting nucleic acids through the use of at least two electrodes where one nucleic acid is immobilized to a first electrode and is allowed to come into contact with a solution that comprises a complementary nucleic acid that will form a hybridization complex with the immobilized nucleic acid, or probe. Additionally, the Examiner asserted that Thorp et al., discloses that the electronic signal may be characteristic of any electrochemical method, including cyclic voltammetry, normal pulse voltammetry chronoamperometry, and square-wave voltammetry. The Examiner concluded, therefore, that the disclosure of Thorp et al. is considered to anticipate, or in the alternative, render obvious the claimed methods of measuring the current or voltage.

According to Thorp et al., hybridization is detected by the use of redox-active molecules being bound to the biopolymers to be detected. In contrast, according to the present invention, such redox-active molecules are not necessary to detect a hybridization of complementary biopolymers. In order to distinguish the present invention from Thorp et al., Applicants' claim 1 recites "measuring a direct change in the voltage and/or current" (emphasis added). The specification defines "measured directly" to mean that redox-active molecules are not necessary to practice the methods of the invention (see page 2, lines 35-37).

"Defining the problem in terms of its solution reveals improper hindsight in the selection of the prior art relevant to obviousness" (*Monarch Knitting Machinery Corp. v. Fukuhara Industrial & Trading Co., Ltd.*, 139 F.3d 977, 45 USPQ2d 1977 (Fed. Cir. 1998)). The Examiner has used improper hindsight in rejecting claims 1-13 over the Thorp et al. reference. The cited reference does not teach or suggest a method of detecting a biopolymer in a liquid that does not require the presence of a redox-active molecule.

In addition, according to *Interconnect Planning Corp. v. Feil* (744 F.2d 1132, 227 USPQ 543 (Fed. Cir. 1985)), "[i]t is [an] error to reconstruct the patentee's claimed invention from the prior art by using the patentee's claim as a 'blueprint'." The cited reference does not teach or

Applicant : Wolf Bertling et al.
Serial No. : 10/069,840
Filed : June 26, 2002
Page : 9 of 9

Attorney's Docket No.: 10848-021US1 / 422073GA-go

suggest that a biopolymer can be detected and quantitated without the presence of a redox-active molecule. Therefore, Thorpe et al. does not teach or suggest the claimed invention. In view of the remarks herein, Applicants respectfully request that the rejection of claims 1-9 and 13 under 35 U.S.C. §102/103 be withdrawn.

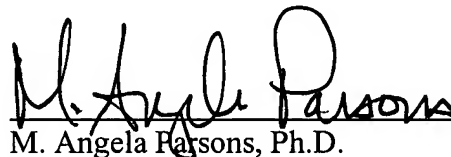
CONCLUSION

Applicants respectfully request that claims 1-13 be allowed. Enclosed is a \$475 check for the Three-Month Petition for Extension of Time fee. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

Date:

January 28, 2004



M. Angela Parsons, Ph.D.
Reg. No. 44,282

Fish & Richardson P.C., P.A.
60 South Sixth Street
Suite 3300
Minneapolis, MN 55402
Telephone: (612) 335-5070
Facsimile: (612) 288-9696